14. (Amended) The method of Claim 13, wherein said derivative of L-arginine is selected from the group consisting of hydroxylated L-arginine, di-, tri- or tetra-peptides having L-arginine or hydroxylated L-arginine at the amino terminal end, esters of L-arginine, esters of hydroxylated L-arginine, amides of L-arginine, amides of hydroxylated L-arginine, L-homoarginine, hydroxylated L-homoarginine, esters of L-homoarginine, esters of hydroxylated L-arginine, amides of L-homoarginine and amides of hydroxylated L-arginine.

a2
Sub C1

REMARKS

Claims 1-25 are pending in the application. Non-elected Claims 26-32 have been withdrawn from consideration. By the present Amendment, inadvertent typographical errors have been corrected in Claims 2 and 14. Specifically, the spelling of "L-homoarginine" has been corrected. No issue of new matter is presented.

Independent Claim 1 recites a method for treating sexual dysfunction in a male patient comprising topically administering to the genitals of said patient an effective amount of L-arginine or a derivative or L-arginine and an effective amount of an antioxidant.

Independent Claim 13 recites a method for treating sexual dysfunction in a female patient comprising topically administering to the genitals of said patient an effective amount of L-arginine or a derivative or L-arginine and an effective amount of an antioxidant.

Claims 1-25 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Duckett et al. '824 in combination with Hechtman '753 by itself or in further combination with Wysor '002. It is submitted that independent Claims 1 and 13, and the claims that depend therefrom, are patentable over the prior art of record.

Duckett et al. '824 discloses orally administered compositions containing L-arginine, ginseng and Zizyphi fructus for treating sexual dysfunction. Duckett et al. '824 fails to teach or suggest any type of topical administration, and further fails to teach or suggest topical administration to the genitals of a patient, as presently claimed. Furthermore, it is submitted that the ginseng disclosed by Duckett et al. '824 is not an antioxidant provided in an effective amount, as presently claimed.

Hechtman '753 is cited to allegedly overcome the shortcomings of Duckett et al. '824. Duckett et al. '824 teaches oral administration to a patient, while Hechtman '753 teaches topical administration to the gastrointestinal tract of a patient. One skilled in the art of topically

applied compositions would not look to the art of orally administered compositions. Therefore, it is submitted that the references represent non-analogous art, and the rejection based on the combination of Duckett et al. '824 and Hechtman '753 is improper and should be withdrawn.

Furthermore, even if Duckett et al. '824 and Hechtman '753 could properly be combined, such a combination would not result in the presently claimed methods. Duckett et al. '824 teaches oral administration. Hechtman '753 teaches topical administration of L-arginine without an antioxidant to the anus or other portion of the gastrointestinal tract. Neither Duckett et al. '824 nor Hechtman '753 teach or suggest administration of a compound to the genitals of a patient, as presently claimed.

In addition, Duckett et al. '824 teaches that it is the combination of L-arginine, ginseng, and Zizyphi fructus together that, when taken orally, generates enough NO to have an effect on muscle relaxation. Column 4, lines 12-16 of Duckett et al. '824, states that NO generation from L-arginine alone "would be insufficient to produce the desired result". In contrast, the presently claimed methods recite the administration of an effective amount of L-arginine or a derivative thereof. "Effective amount" is defined in the specification as being enough to bring about the desired amount of blood flow to the erectile tissue (see page 7, lines 7-9). In contrast, as taught at column 4, lines 12-16, Duckett et al. '824 does not use an amount of L-arginine effective to bring about the desired blood flow. Instead, the reference teaches that L-arginine cannot be used effectively alone.

As a further distinction, Duckett et al. '824 does not teach that ginseng is used as an antioxidant as claimed in the present invention. According to the present invention, the recited antioxidant is used in an effective amount that converts superoxide molecules to hydrogen peroxide and oxygen, and is used in the topically applied composition in an amount that minimizes peroxynitrite damage caused by L-arginine or derivatives thereof. (See page 6, lines 15-17; page 7, lines 6-9.) In contrast, ginseng is used in the orally administered compositions of Duckett et al. '824 as one component of a three component synergistic blend that causes NO stimulation in the gastrointestinal tract. One skilled in the art would not be led by the teachings of Hechtman '753 and Duckett et al. '824 to topically apply a combination of an effective amount of L-arginine or a derivative thereof and an effective amount of antioxidant to the genitals of a patient as presently claimed.

Wysor '002 is cited as teaching administration of prostaglandin to enhance female sexual response. Wysor '002 does not teach or suggest the application of L-arginine or derivatives thereof and an antioxidant to the genitals of a patient, as presently claimed. No teaching or suggestion is provided in Wysor '002, or any other prior art of record, that the prostaglandin of Wysor '002 could be replaced with L-arginine (or a derivative thereof) or an antioxidant. Furthermore, with respect to Claim 1 which is directed to topical administration to male patients, Wysor '002 is limited to female patients.

It would not have been obvious to topically apply the compositions of Duckett et al. '824 to the genitals of a patient, based upon the teachings of Hechtman '753 and Wysor '002. For a combination of references to be properly applied, there must be some suggestion of combination in the references themselves. Applicants respectfully submit such motivation is lacking here. Duckett et al. '824 does not teach or remotely suggest topical application. Hechtman '753 teaches topical application of a different formulation to a different body part to achieve a different ultimate result (i.e., relieving involuntary spasms versus engorgement of erectile tissue). Wysor '002 merely discloses application of prostaglandin to enhance female sexual response. Only through the improper use of hindsight can the references be combined in the manner suggested in the Office Action to arrive at the presently claimed invention. Accordingly, it is submitted that the rejection based upon Duckett et al. '824, Hechtman '753 and Wysor '002 is improper and should be withdrawn.

Even if the references were combinable in the manner suggested in the Office Action, which Applicants do not concede, the result would not be the present invention. None of the references teach the application of effective amounts of L-arginine (or derivatives thereof) and effective amounts of an antioxidant to the genitals of a patient.

Claims 13-25 are further rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Duckett et al. '824 in combination with Hechtman '753, by itself or in further combination with Wysor '002 and further in view of Chobanian et al '847. This rejection is respectfully traversed.

The comments made above regarding Duckett et al. '824, Hechtman '753, and Wysor '002 apply equally here. The citation to Chobanian et al. '847 does not overcome the shortcomings of these references. There is no teaching, suggestion or motivation in the prior art of record to combine the Duckett et al. '824, Hechtman '753, Wysor '002 and Chobanian et

al '847 references in the manner suggested in the Office Action. Instead, it is submitted that the Office Action relies upon Applicants' claims as a blueprint to piece together features found separately in the prior art. Accordingly, the rejection improperly relies on hindsight and should be withdrawn.

Furthermore, even if the references could properly be combined, antioxidants are taught by Chobanian et al. '847 as being NO catabolism inhibitors, not as protecting against peroxynitrite damage. None of the references teach or suggest the use of an effective amount of an antioxidant for the protection of tissue from oxidative damage as contemplated by the present invention. None of the references alone, or in combination, teach or suggest topical administration to the genitals of a patient of a composition comprising an effective amount of L-arginine or a derivative thereof and an effective amount of an antioxidant as recited in Claims 1 and 13.

The dependent claims recite additional features which further serve to distinguish over the prior art.

Dependent Claims 2 and 14 recite methods wherein said derivative of L-arginine is selected from the group consisting of hydroxylated L-arginine, di-, tri- or tetra-peptides having L-arginine or hydroxylated L-arginine at the amino terminal end, esters of L-arginine, esters of hydroxylated L-arginine, amides of L-arginine, amides of hydroxylated L-arginine, L-homoarginine, hydroxylated L-homoarginine, esters of L-homoarginine, esters of hydroxylated L-arginine, amides of L-homoarginine and amides of hydroxylated L-arginine. The use of such specific L-arginine derivatives in combination with an antioxidant for application to the genitals of a patient is not taught or suggested by the prior art of record.

Dependent Claims 3-5 and 15-17 recite specific esters of L-arginine. The use of such esters in combination with an antioxidant for application to the genitals of a patient is not taught or suggested by the prior art of record.

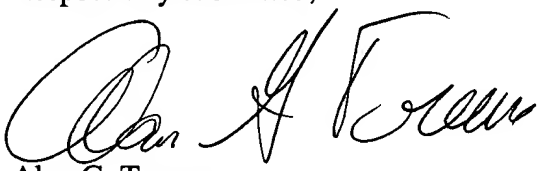
Dependent Claims 6, 7, 18 and 19 recite that the antioxidant is ascorbic acid or derivatives thereof (Claims 6 and 18); and that the antioxidant is a combination of ascorbic acid and ascorbic acid palmitate (Claims 7 and 19). The use of such specific antioxidants in combination with L-arginine or derivatives thereof for application to the genitals of a patient is not taught or suggested by the prior art of record.

Dependent Claims 11 and 23 recite a method wherein said effective amounts are those amounts necessary to cause the desired level of blood flow to erectile tissue while minimizing peroxynitrite levels. This combination is not taught or suggested by the prior art of record.

In view of the foregoing remarks, it is submitted that Claims 1-25 are patentable over the prior art of record. Accordingly, an early Notice of Allowance of this application is respectfully requested.

In the event that any outstanding matters remain in connection with this application, the Examiner is invited to telephone the undersigned at (412) 263-4340 to discuss such matters.

Respectfully submitted,



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Marked-up Version of Claims

2. (Amended) The method of Claim 1, wherein said derivative of L-arginine is selected from the group consisting of hydroxylated L-arginine, di-, tri- or tetra-peptides having L-arginine or hydroxylated L-arginine at the amino terminal end, esters of L-arginine, esters of hydroxylated L-arginine, amides of L-arginine, amides of hydroxylated L-arginine, L-homoarginine, hydroxylated L-homoarginine, esters of L-homoarginine, esters of hydroxylated L-arginine, amides of [L-homoargine] L-homoarginine and amides of hydroxylated L-arginine.

14. (Amended) The method of Claim 13, wherein said derivative of L-arginine is selected from the group consisting of hydroxylated L-arginine, di-, tri- or tetra-peptides having L-arginine or hydroxylated L-arginine at the amino terminal end, esters of L-arginine, esters of hydroxylated L-arginine, amides of L-arginine, amides of hydroxylated L-arginine, L-homoarginine, hydroxylated L-homoarginine, esters of L-homoarginine, esters of hydroxylated L-arginine, amides of [L-homoargine] L-homoarginine and amides of hydroxylated L-arginine.